UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/502,235	07/22/2004	Małgorzata Anna Kisielow	1-32330A/FMI	9191

1095 7590 06/01/2007

NOVARTIS
CORPORATE INTELLECTUAL PROPERTY
ONE HEALTH PLAZA 104/3
EAST HANOVER, NJ 07936-1080

EXAMINER	
SAJJADI, FEREYDOUN GHOTB	
ART UNIT	PAPER NUMBER
1633	
MAIL DATE	DELIVERY MODE
06/01/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/502,235	KISIELOW ET AL.	
	Examiner	Art Unit	
	Fereydoun G. Sajjadi	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 April 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-23* is/are pending in the application.

4a) Of the above claim(s) *13 and 21-23* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-12 and 14-20* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claim Status

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicants' submission filed on April 10, 2007 that includes a response to the Advisory action dated March 7, 2007 has been entered. Claims 1-23 remain pending in the application. Claim 1 has been amended. No claims were cancelled and no claims were newly added. Claims 13 and 21-23 remain withdrawn from consideration, as drawn to non-elected inventions.

Claims 1-12, and 14-20 are under current examination.

New Claim Rejections - 35 USC § 112- Second Paragraph

Applicants' claim amendments have necessitated the following new grounds of rejection.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-12 and 14-20 are newly rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 is unclear. Step (a) of claim 1 recites: "determining from a gene product of interest, a specific isoform of interest from said gene product". As said determination requires a plurality of gene products, it is not clear how a single gene product may lead one to the various isoforms. The determination can be made from all the products of a gene of interest. Claims 2-12 and 14-20 depend from claim 1 and have been included in the rejection, as they do not contain language obviating the ground of rejection.

Response to Claim Rejections - 35 USC § 112, Written Description

Claims 1-12 and 14-20 stand rejected under 35 U.S.C. §112, first paragraph, as failing to comply with the written description requirement. The rejection set forth on pp. 3-5 of the previous office action dated October 10, 2006 is maintained for claims 1-12 and 14-20, for reasons of record.

Applicants disagree with the rejection, stating that Applicants have amended independent claim 1 to include the additional first step of "determining, from a gene product of interest, a specific isoform of interest from said gene product, and isoforms of said gene product not of interest.", and have ensured that practitioners of the claimed methods of the invention possess knowledge of the isoforms of the gene products of interest. Additionally arguing, that the gene products themselves (e.g., the encoded proteins) are not essential to the claimed methods of the invention, and that there is no substantial variation within the claimed genus- i.e., practitioners of the claimed invention are interested in the nucleic acids of the present claims only in terms of the presence and number of their isoforms, and the nucleic acid sequences thereof, and not in terms of the gene products encoded thereby. Applicants also reiterate the applicability of the following from Example 18 of the Written Description Guidelines: "The art indicates that there is no substantial variation within the genus because there are a limited number of ways to practice the process steps of the claimed invention," and posit that the steps of the claimed methods are similarly applied to all nucleic acids with one or more isoforms, irrespective of the gene products encoded thereby. Applicants also reiterate prior arguments that a practitioner of the methods of the invention only needs to possess knowledge relating to her gene product of interest (as opposed to knowledge about every possible gene product within the claimed methods), and that one would already possess said information before employing the presently claimed methods.

Applicants' arguments have been fully considered, but are not found persuasive. As previously indicated, the instantly claimed method of expressing a specific isoform of any gene product, in any cell, absent other isoforms of said gene product, comprises introducing into said cell a ds RNA having at least 95% sequence identity to a common nucleic acid sequence shared by two or more isoforms of said gene product. As such (and as stated by Applicants in the foregoing), the claims require specific knowledge of the sequences for the desired isoforms of

any gene product of interest, whether endogenous to said cell or isoforms that may be exogenous in origin, to determine the nature of the sequences that would constitute a common and shared nucleic acid. The specification defines isoform "to encompass gene products that are produced as a result of differential gene splicing as well as from the use of alternative transcription start sites. In addition, ...the term isoforms include any closely related sequences and therefore may include a mutated gene in a cell" (p. 10, lines 30-31, bridging p. 11, lines 1-4). The specification discloses only the Shc gene family as exemplary for isoforms of a signaling adaptor/scaffold gene product (Example 1, p. 17) with ShcA, as exemplary for the desired isoform (line 6, p.18) and specifically describe the use of 21-mer oligonucleotide pairs as siRNAs of Shc (lines 28-29, p. 18). However, the specification provides no description of the substantial number of genes that can express more than one isoform, or have closely related sequences thereto, in any cell, as claimed. The specification is further devoid of any description for a desired isoform replacing a mutant isoform or a tumor suppressive mutant isoform in a cell.

The method of the instant invention requires and is dependent on RNA interference by double stranded ribonucleic acid, that must be designed in a sequence specific manner, to form a specific secondary structure, and empirically tested to determine whether any particular double stranded sequence having 95% sequence identity to a sequence commonly shared by the different isoforms would result in proper suppression of expression of all said isoforms. The instant claims are directed to expressing a specific isoform of any gene product, whereas the limited information provided by the specification is for the Shc family and the design of an siRNA, only applicable to the Shc genes. Applicants have acknowledged that a skilled practitioner may utilize the instantly claimed method, when knowledge regarding the gene of interest, the isoforms and the sequences encoded thereby is already possessed. However, such knowledge is in fact absent from the instant specification, unless said practitioner wished to specifically express an isoform of the Shc gene.

With regards to Example 18 of the Written Description Guidelines, wherein: "The art indicates that there is no substantial variation within the genus because there are a limited number of ways to practice the process steps of the claimed invention," such is not applicable to the instant case, where the expression of numerous isoforms of a multitude of genes may need to be suppressed by at least one siRNA molecule and said suppression would require specific

knowledge of shared sequences among the different isoforms of a gene. The instant claims embrace the sequences for the isoforms of a genus of any gene, thus encompassing substantial sequence variation within the genus.

Thus, the rejection of claims 1-12 and 14-20, is maintained for reasons of record and the foregoing discussion.

Reply to Claim Rejections - 35 USC § 112-Scope of Enablement

Claims 1-12 and 14-20 were rejected under 35 U.S.C.§112, first paragraph, because the specification does not reasonably provide an enablement for the full scope of the invention, in the previous office action dated October 10, 2006. In view of Applicants' amendment of the claims, altering the scope of the claim invention, and new rejections set forth below, the previous rejection of the claims is hereby withdrawn. To the extent that Applicants' arguments are applicable to claim rejections outstanding in the application, the following remarks follow:

Applicants disagree, that there remain additional issues regarding the unpredictability of attenuating expression of numerous target genes by RNAi in different cell types for which adequate structural details need to be determined, and which would require undue experimentation, stating that by the addition of a first step to claim 1, (i.e. determining, from a gene product of interest, a specific isoform of interest from said gene product, and isoforms of said gene product not of interest, practitioners ascertain which inhibitory ribonucleic acid sequences (which overlap between desired and undesired isoforms) are most likely to successfully knock down the undesired isoforms and leave the mismatched, desired isoforms remaining.

Applicants' arguments have been fully considered, but are not found persuasive. In response, Applicants are directed to the foregoing commentary regarding the requirement to characterize the isoforms to a gene product of interest, and to further test various siRNA sequences for their ability to specifically inhibit all isoforms of the gene. In addition, the instantly claimed method requires the complete suppression of expression of all isoforms, variants, mutants and closely related sequences of a gene product and, the post-filing art of record clearly suggests that administering dsRNA, either *in vitro* or *in vivo*, to attenuate

expression of target genes is not a reproducible or predictable art.

New Claim Rejections - 35 USC § 101-Lack of Utility

Applicants' claim amendments have in part necessitated the following new grounds of rejection.

35 U.S.C. § 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Definitions:
[from REVISED INTERIM UTILITY GUIDELINES TRAINING MATERIALS; repeated from http://www.uspto.gov/web/menu/utility.pdf]

"Credible Utility" - Where an applicant has specifically asserted that an invention has a particular utility, that assertion cannot simply be dismissed by Office personnel as being "wrong". Rather, Office personnel must determine if the assertion of utility is credible (i.e., whether the assertion of utility is believable to a person of ordinary skill in the art based on the totality of evidence and reasoning provided). An assertion is credible unless (A) the logic underlying the assertion is seriously flawed, or (B) the facts upon which the assertion is based is inconsistent with the logic underlying the assertion. Credibility as used in this context refers to the reliability of the statement based on the logic and facts that are offered by the applicant to support the assertion of utility. A *credible* utility is assessed from the standpoint of whether a person of ordinary skill in the art would accept that the recited or disclosed invention is currently available for such use. For example, no perpetual motion machines would be considered to be currently available. However, nucleic acids could be used as probes, chromosome markers, or forensic or diagnostic markers. Therefore, the credibility of such an assertion would not be questioned, although such a use might fail the *specific* and *substantial* tests (see below).

"Specific Utility" - A utility that is *specific* to the subject matter claimed. This contrasts with a *general* utility that would be applicable to the broad class of the invention. For example, a claim to a polynucleotide whose use is disclosed simply as a "gene probe" or "chromosome marker" would not be considered to be *specific* in the absence of a disclosure of a specific DNA target. Similarly, a general statement of diagnostic utility, such as diagnosing an unspecified disease, would ordinarily be insufficient absent a disclosure of what condition can be diagnosed.

"Substantial utility" - a utility that defines a "real world" use. Utilities that require or constitute carrying out further research to identify or reasonably confirm a "real world" context of use are not substantial utilities. For example, both a therapeutic method of treating a known or newly discovered disease and an assay method for identifying compounds that themselves have a "substantial utility" define a "real world" context of use. An assay that measures the presence of a material which has a stated correlation to a predisposition to the onset of a particular disease condition would also define a "real world" context of use in identifying potential candidates for

preventive measures or further monitoring. On the other hand, the following are examples of situations that require or constitute carrying out further research to identify or reasonably confirm a "real world" context of use and, therefore, do not define "substantial utilities":

A. Basic research such as studying the properties of the claimed product itself or the mechanisms in which the material is involved.

B. A method of treating an unspecified disease or condition. (Note, this is in contrast to the general rule that treatments of specific diseases or conditions meet the criteria of 35 U.S.C. 101.)

C. A Method of assaying for or identifying a material that itself has no "specific and/or substantial utility".

D. A method of making a material that itself has no specific, substantial, and credible utility.

E. A claim to an intermediate product for use in making a final product that has no specific, substantial, and credible utility.

Note that "throw away" utilities do not meet the tests for a *specific* or *substantial* utility. For example, using transgenic mice as snake food is a utility that is neither specific (all mice could function as snake food) nor substantial (using a mouse costing tens of thousands of dollars to produce as snake food is not a "real world" context of use). Similarly, use of any protein as an animal food supplement or a shampoo ingredient are "throw away" utilities that would not pass muster as specific or substantial utilities under 35 U.S.C. ' 101. This analysis should, or course, be tempered by consideration of the context and nature of the invention. For example, it a transgenic mouse was generated with the specific provision of an enhanced nutrient profile, and disclosed for use as an animal food, then the test for specific and substantial *asserted* utility would be considered to be met.

"Well established utility" - a specific, substantial, and credible utility which is well known, immediately apparent, or implied by the specification's disclosure of the properties of a material, alone or taken with the knowledge of one skilled in the art. "Well established utility" does not encompass any "throw away" utility that one can dream up for an invention or a nonspecific utility that would apply to virtually every member of a general class of materials, such as proteins or DNA. If this is the case, any product or apparatus, including perpetual motion machines, would have a "well established utility" as landfill, an amusement device, a toy, or a paper weight; any carbon containing molecule would have a "well established utility" as a fuel since it can be burned; any protein would have well established utility as a protein supplement for animal food. This is not the intention of the statute.

See also the MPEP § 2107 - 2107.02.

Claims 1-12 and 14-20 are rejected under 35 U.S.C.§ 101 because the claimed invention is not supported by either a specific or substantial asserted utility or a well established utility.

The claims are directed to an *in vitro* method of expressing a specific isoform of a gene product in a cell absent undesired isoform products of said gene, said method comprising: exposing a mammalian cell to at least one nucleic acid, said nucleic acid having at least 95% sequence identity to a common nucleic acid sequence shared by two or more isoform products of

said gene; and introducing an expression vector encoding a specific isoform of said gene product into said mammalian cell.

The instant specification discloses that although "multiple isoforms are expressed in the same cell at the same time, the expression level and pattern of each isoform may vary with cell type and developmental stage, making the study of each isoform confusing and difficult." (lines 18-20, p. 1). The specification further states:" There is a need in the art for a system to evaluate gene function, in particular for the evaluation of isoform function in mammalian cells, as well as therapies dependent on dsRNA inhibition of closely related mRNAs in mammalian cells, and this invention meets that need." (lines 21-24, p. 3). Therefore, the instantly claimed method provides a means to test and evaluate both RNAi approaches and to study a specific isoform product of a gene, in the absence of other "interfering" isoforms. Applicants have further stated on the record: "The present claims, in their amended state, describe *in vitro* analytical techniques best suited for the study of certain desired isoforms of gene products of interest".

Therefore, the foregoing constitutes using the invention as an object of research in order to determine the function or effects of a specific isoform of interest, or to evaluate dsRNA inhibition, and does not meet the requirement for a substantial utility. As indicated in the utility guidelines above, utilities that require or constitute carrying out further research to identify or reasonably confirm a "real world" context of use are not substantial utilities. As the instantly claimed method lacks a substantial utility, the invention further lacks a well established utility.

New Claim Rejections - 35 USC § 112-Lack of Enablement

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-12 and 14-20 are rejected under 35 U.S.C. §112, first paragraph. Specifically, as the claimed invention is not supported by a substantial asserted utility or a well established

utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention without further experimentation.

Claim 1-12 and 14-20 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. The specification is not enabling for an *in vitro* method of expressing a specific isoform of any gene product in a cell absent undesired isoforms of said gene, by exposing said cell to dsRNA, and wherein said cell is a cancer cell as claimed.

This rejection is based on the absence of an enabling disclosure for the specific expression of a single isoform of any gene in a cell using RNAi technology, in the absence of information regarding the sequences for the various isoforms of a gene. The deficiency was identified by the Office after analysis of the disclosure provided in the instant application. In determining whether Applicant's claims are enabled, it must be found that one of skill in the art at the time of invention by Applicant would not have had to perform "undue experimentation" to make and/or use the invention claimed. Factors to be considered in determining whether a disclosure meets the enablement requirement of 35 USC 112, first paragraph, have been described by the court in *In re Wands*, 8 USPQ2d 1400 (CA FC 1988). *Wands* states at page 1404:

> "Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized by the board in Ex parte Forman. They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims."

The Office has analyzed the specification in direct accordance to the factors outlined in *In re Wands*. MPEP § 2164.04 states: "[W]hile the analysis and conclusion of a lack of enablement are based on the factors discussed in MPEP § 2164.01(a) and the evidence as a whole, it is not necessary to discuss each factor in the written enablement rejection."

The instant claims encompass a method of expressing a specific isoform of a gene of interest in any cell absent undesired isoforms of said gene; said method comprising exposing a cell to at least one nucleic acid, said nucleic acid having at least 95% sequence identity to a common nucleic acid sequence shared by two or more isoforms of said gene; and introducing an expression vector encoding a specific or desired isoform of said gene into said mammalian cell

The specification fails to disclose adequate representations of desired isoforms of any gene products, in any type of cell. The specification merely discloses the three isoforms of the Shc gene and a combination of RNAi and plasmid mediated gene expression for transfection in HeLa cells *in vitro* (Examples 1-3, pp. 17-25), resulting in the inhibition and subsequent expression of an isoform of a Shc gene product. However, the specification provides no additional examples of isoforms of a gene product.

The unpredictability of attenuating expression of a target gene in all types of cells, including mammalian cells, by RNA interference (RNAi) is evident in prior and post-filing art. While it is recognized that introduction of dsRNA that is targeted to a specific gene may result in attenuation of expression of the targeted gene, the degree of attenuation and the length of time that attenuation is achieved is not predictable. Caplen et al. (Gene, 252:95-105, 2000; of record) provide evidence of the unpredictability of dsRNA attenuation of a targeted gene in vertebrate cells *in vitro*. Caplen et al. report that although dsRNA inhibits gene expression in cultured *Drosophila* cells, screening of three commonly used cell lines from three different species: human, hamster, and mouse, using cells expressing transgenes both transiently and permanently, produced mixed results.

Given these teachings, the skilled artisan would not know *a priori* whether introduction of dsRNA or hairpin nucleic acids into any type of cell, would result in successful attenuation/inhibition of a target gene. In fact, the prior art teaches that successful delivery of nucleotide sequences to a target cell *in vitro*, such that the oligonucleotide provides the requisite biological effect to the target cells/tissues/organs, must be determined empirically.

The specification does not provide the guidance required to overcome the art-recognized unpredictability of dsRNA for use in RNA interference in various types of cells. Therefore, in view of the lack of teachings or guidance provided by the specification with regard to expression restricted to only one specific isoform product of any gene having multiple isoforms, in any cell

type, and for the specific reasons cited above, it would have required undue experimentation for an Artisan of skill to make and use the claimed invention. Hence, absent a strong showing by Applicant, in the way of specific guidance and direction, and/or working examples demonstrating the same, such invention as claimed by Applicant is not enabled.

Response to Claim Rejections - 35 USC § 102

Claims 1-12 and 14-20 stand rejected under 35 USC § 102(e), as anticipated by Tuschl et al. (U. S. Patent Application No.: 2004/0259247, filed Nov. 29, 2001). The rejection set forth on pp. 8-10 of the previous office action dated October 10, 2006 is maintained for claims 1-12 and 14-20, for reasons of record.

Applicants disagree with the rejection, stating that not every element of claims 1-12 and 14-20 is met by the Tuschl et al. reference. Specifically, arguing that the RNAi methods disclosed in the Tuschl et al. reference describes using RNAi to inhibit the expression of endogenous target genes, thereby knocking them out (i.e., suppressing their function); on the other hand, the present invention contemplates inhibiting isoforms of a gene of interest, while protecting isoforms of interest of the gene of interest. Additionally arguing that the Tuschl reference pertains to therapeutic treatment, as opposed to the kind of investigation and analysis engendered by the present method claims.

Applicants arguments have been fully considered, but not found persuasive. As previously indicated, the invention of Tuschl et al. utilizes double stranded RNA (siRNA) for RNA interference for sequence-specific post transcriptional gene silencing (Abstract), and further teach that their method may be used in analytic procedures, e.g. in the functional and /or phenotypical analysis of gene expression profiles and/or proteomes (paragraph [0036, column 2, p. 3). "Using RNAi based knockout technologies, the expression of an endogenous target gene may be inhibited in a target cell" (paragraph [0037], column 2, p. 3), further, "capable of inhibiting the expression of at least one endogenous target gene. "The endogenous gene may be complemented by an exogenous target nucleic acid coding for the target protein or a variant or mutated form of the target protein, e.g. a gene or a cDNA" (paragraph [0038], column 2, p. 3). Thus, the teachings of Tuschl et al. are not limited to therapeutic treatment. Applicants should further note that exogenous and endogenous target genes described by Tuschl et al. are

equivalent to specific isoforms of interest and other isoforms of a gene product not of interest, respectively, as the exogenous target nucleic acid is encoding the endogenous target protein, and hence is capable of complementation. As stated by Tuschl et al. the complementation may be achieved by an exogenous target nucleic acid coding for the endogenous gene; i.e. the endogenous and exogenous target nucleic acids have identical sequences.

In further response to applicant's argument that the Tuschl reference pertains to therapeutic treatment, as opposed to the kind of investigation and analysis engendered by the present method claims, a recitation of the intended use of the claimed invention must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. If the prior art structure is capable of performing the intended use, then it meets the claim.

Therefore, the rejection of claims 1-12 and 14-20, is maintained for reasons of record and the foregoing discussion.

Conclusion

Claims 1-12 and 14-20, are not allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Fereydoun G. Sajjadi whose telephone number is **(571) 272-3311**. The examiner can normally be reached Monday through Friday, between 7:00-4:00 pm EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph Woitach can be reached on **(571) 272-0739**. The fax phone number for the organization where this application or proceeding is assigned is **(571) 273-8300**. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989).

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR

system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at **866-217-9197** (toll-free).

For all other customer support, please call the USPTO Call Center (UCC) at **(800) 786-9199**.

Fereydoun G. Sajjadi, Ph.D.
Examiner, USPTO, AU 1633

ANNE M. WEHBE' PH.D
PRIMARY EXAMINER